## (19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 20 January 2005 (20.01.2005)

PCT

(10) International Publication Number WO 2005/004884 A3

(51) International Patent Classification7: A61P 9/08, 9/10, 9/12

A61K 33/00,

(21) International Application Number:

PCT/US2004/022232

(22) International Filing Date:

9 July 2004 (09.07.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/485,959 60/511,244 9 July 2003 (09.07.2003)

US 14 October 2003 (14.10.2003) US

(71) Applicants (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by THE SECRETARY, DE-PARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, Suite 325, 6011 Executive Boulevard. Rockville, MD 20852-3804 (US). THE BOARD OF SU-PERVISORS OF LOUISIANA STATE UNIVERSITY AND AGRICULTURAL AND MECHANICAL COL-LEGE, ACTING THROUGH LOUISIANA STATE UNIVERSITY HEALTH SCIENCES CENTER IN SHREVEPORT [US/US]; 1501 Kings Highway, Shreveport, LA 71130 (US). UNIVERSITY OF ALABAMA RESEARCH FOUNDATION [US/US]; AB 1120G, 1530 3rd Avenue South, Birmingham, AL 35294-0111 (US). LOMA LINDA UNIVERSITY [US/US]; Anderson Street and Barton Road, Loma Linda, CA 92350 (US). WAKE FOREST UNIVERSITY [US/US]; Department of Physics, 208 Olin Physical Laboratory, Box 7507, 1834 Wake Forest University, Winston-Salem, NC 27109-7507 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): GLADWIN, Mark. T. [US/US]; 4927 Nebraska, Avenue, Northwest, Washington, DC 20008 (US). SCHECHTER, Alan, N. [US/US]; 5405 Beech Avenue, Bethesda, MD 20814 (US). LEFER, David, J. [US/US]; 5035 Beechwood Hills Drive, Shreveport, LA 71107 (US). PATEL, Rakesh, P. [GB/US]; 4172 River Walk Lane, Birmingham, LA 35294 (US). HUNTER, Christian, J. [US/US]; National Institutes of Health, Critical Care/NIDDK, 10 Center Drive, Building 10, Room 5D45, Bethesda, MD 20892 (US). POWER, Gordon, G. [US/US]; 1431 Henrietta Street, Redlands, CA 92373 (US). KIM-SHAPIRO, Daniel, B. [US/US]; 2065 Craig Street, Winston-Salem, NC 27103 (US). PLUTA, Ryszard [US/US]; National Institutes of Health NINDS, Building 10, Room 5D37, 10 Center Drive, MSC 1414, Bethesda, MD 20892-1414 (US). OLDFIELD, Edward, H. [US/US]; P.O. Box 309, Philomont, VA 22131 (US).

- (74) Agent: HARDING, Tanya, M.; Klarquist, Sparkman, LLP, Suite 1600, One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM). European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

## Published:

with international search report

(88) Date of publication of the international search report: 21 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF NITRITE SALTS FOR THE TREATMENT OF CARDIOVASCULAR CONDITIONS

(57) Abstract: It has been surprisingly discovered that administration of nitrite to subjects causes a reduction in blood pressure and an increase in blood flow to tissues. The effect is particularly beneficial, for example, to tissues in regions of low oxygen tension. This discovery provides useful treatments to regulate a subject's blood pressure and blood flow, for example, by the administration of nitrite salts. Provided herein are methods of administering a pharmaceutically-acceptable nitrite salt to a subject, for treating, preventing or ameliorating a condition selected from: (a) ischemia-reperfusion injury (e.g., hepatic or cardiac or brain ischemiareperfusion injury); (b) pulmonary hypertension (e.g., neonatal pulmonary hypertension); or (c) cerebral artery vasospasm.

